The possible mechanisms of ginseng saponins on the inhibition of development of morphine tolerance and physical dependence were investigated in the aspects of morphine metabolism by morphine 6-dehydrogenase. Administration of morphine causes a reduction of non-protein sulfhydryl contents in liver, because morphinone is metabolized from morphine by morphine 6-dehydrogenase conjugates with sulfhydryl compounds. However, ginseng saponins inhibited the activity of morphine 6-dehydrogenase which catalized the production of morphinone from morphine. In addition, ginseng saponins inhibited the reduction of non-protein sulfhydryl levels by increasing the level of hepatic glutathione. These results suggest that the dual action of the above plays an important role in the inhibition of development of morphine tolerance and physical dependence. On the other hand, it was observed that less polar components of ginseng saponins with parent structures were more active components in vitro.